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(FILE 'HOME' ENTERED AT 12:28:20 ON 11 JAN 2005)

FILE 'STNGUIDE' ENTERED AT 12:28:25 ON 11 JAN 2005

FILE 'HOME' ENTERED AT 12:28:30 ON 11 JAN 2005

FILE 'MEDLINE, CAPLUS' ENTERED AT 12:28:57 ON 11 JAN 2005

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L1         27630 S ERYTHROPOIETIN
L2        190189 S CHO OR COS OR BHK OR NAMALWA OR HELA
L3        362977 S INSULIN
L4        639376 S GLUCOSE
L5             1 S L1 (L) L2 (L) L3 (L) L4
```

=> d an ti so au ab pi l5

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:261609 CAPLUS
DN 129:104852
TI Serum-free medium used for production of recombinant human erythropoietin
SO Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
CODEN: JYKYEL; ISSN: 1000-5501
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB Various additives of serum-free medium suitable to **CHO** cells were screened based on the consumption of medium compns. of C2 cells producing recombinant human **erythropoietin** (Rhuepo). Se, Ethanolamine, lipid, various vitamins, peptone, **insulin**, transferrin and some cytokines were added in a DMEM:F12 (1:1) medium to constitute the serum-free medium named SFM-p. It contained no bovine serum albumin but could support the growth and Rhuepo production of C2 cells. Productivity of Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling bottles. The same studies were conducted in a packed bed bioreactor for C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be maintained in a stable condition of Rhuepo production for 20 days in the bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4 μg/mL of Rhuepo. **Glucose** consumption rate was 21 g per L per day. The highest d. of cells could exceed 3.0 x 107 cells/mL, and Rhuepo could be easily separated from the culture supernatant. Thus, SFM-p can maintain the growth and recombinant human **erythropoietin** production in recombinant C2 cells.

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L1 27630 S ERYTHROPOIETIN
L2 190189 S CHO OR COS OR BHK OR NAMALWA OR HELA
L3 362977 S INSULIN
L4 639376 S GLUCOSE
L5 1 S L1 (L) L2 (L) L3 (L) L4
L6 6 S L1 (L) L2 (L) L3
L7 5 DUP REM L6 (1 DUPLICATE REMOVED)
L8 5 SORT L7 PY

=> d an ti so au ab pi l8 1-5

L8 ANSWER 1 OF 5 MEDLINE on STN
AN 87185843 MEDLINE
TI Binding and internalization of recombinant human erythropoietin in murine erythroid precursor cells.
SO Blood, (1987 May) 69 (5) 1485-90.
Journal code: 7603509. ISSN: 0006-4971.
AU Mufson R A; Gesner T G
AB **Erythropoietin** (EPO) biosynthetically labelled with [35S]cysteine was produced from Chinese hamster ovary (**CHO**) cells containing amplified copies of human EPO cDNA. The glycosylated recombinant [35S]EPO, purified to virtual radiochemical homogeneity, was biologically active. We studied the interaction of this labeled recombinant EPO with erythroid precursor cells from mice made anemic with phenylhydrazine. The [35S]-labeled molecule bound to erythroid precursors in a time- and temperature-dependent manner. The binding was specific for EPO, and neither **insulin**, transferrin, epidermal growth factor, nor multiplication stimulating activity could compete for EPO binding sites. In the presence of 0.2% sodium azide, which blocks 80% to 90% of internalization, the recombinant molecule bound with an apparent Kd of 750 pmol/L and 100 to 200 binding sites per cell at 37 degrees C. Asialo-EPO was a more effective competitor than sialated EPO for the available binding sites. Thus, the enhanced biological specific activity of asialo-EPO could result from its enhanced binding affinity. We also studied recombinant human EPO labeled with 125I and found that it also bound to the erythroid cells in a saturable and specific manner. After 90 minutes of incubation at 37 degrees C, most of the bound [35S]EPO was internalized, whereas most of the [125I]EPO remained on the cell surface. The reduced internalization of the iodinated molecule could account for the previously reported functional deficit associated with iodination.

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:18879 CAPLUS
DN 118:18879
TI Serum-free medium for cultivation of mammalian cells
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
IN Koch, Stefan; Behrendt, Ulrich; Franze, Rienhard; Lorenz, Thomas; Szperalski, Berthold
AB The title medium, which contains no proteins of animal origin, contains recombinant **insulin** from a prokaryote and a water-soluble Fe compound in place of the animal **insulin** and transferrin used in conventional serum-free media. The medium may be used for cultivation of recombinant **CHO** cells containing an **erythropoietin** gene for production of **erythropoietin**. Thus, a medium for **CHO** cells was prepared by mixing equal vols. of Dulbecco's modified Eagle's medium and Nutrient Mixture F-12 and adding biotin 0.2036, recombinant **insulin** 5.0, putrescine 0.1, vitamin B12 0.78, Fe citrate 124 mg/L, hydrocortisone 3.6 μg/L, and poly(vinyl alc.) 1 g/L. The maximum

viable and total cell densities achieved were 15.3 + 10-5 and 25.7 + 10-5/mL, resp., both after 164 h.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 513738	A2	19921119	EP 1992-107997	19920512
	EP 513738	A3	19930505		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	DE 4115722	A1	19921119	DE 1991-4115722	19910514
	JP 05252942	A2	19931005	JP 1992-117275	19920511

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:261609 CAPLUS
DN 129:104852
TI Serum-free medium used for production of recombinant human erythropoietin
SO Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246
CODEN: JYKYEL; ISSN: 1000-5501
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen
AB Various additives of serum-free medium suitable to **CHO** cells were screened based on the consumption of medium compns. of C2 cells producing recombinant human **erythropoietin** (Rhuepo). Se, Ethanolamine, lipid, various vitamins, peptone, **insulin**, transferrin and some cytokines were added in a DMEM:F12 (1:1) medium to constitute the serum-free medium named SFM-p. It contained no bovine serum albumin but could support the growth and Rhuepo production of C2 cells. Productivity of Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling bottles. The same studies were conducted in a packed bed bioreactor for C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be maintained in a stable condition of Rhuepo production for 20 days in the bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4 μg/mL of Rhuepo. Glucose consumption rate was 21 g per L per day. The highest d. of cells could exceed 3.0 x 107 cells/mL, and Rhuepo could be easily separated from the culture supernatant. Thus, SFM-p can maintain the growth and recombinant human **erythropoietin** production in recombinant C2 cells.

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:856280 CAPLUS
TI Serum-free badge for mammalian cell culture
SO Repub. Korea, No pp. given
CODEN: KRXXFC
IN Yoon, Sung Kwan; Ahn, Yong Ho
AB Serum free medium for mammalian cell culture is provided, which supports the growth of cells to the same rate of growth in the medium containing serum. Expression of a recombinant protein in cell culture medium containing serum originated from animal needs more steps for the purification of expressed protein because of many interfering components in the serum. The com. media such as DMEM, HAM, IMDM, or RPMI 1640 are used for a basic medium of a serum free medium (LSF medium). The basic medium of LSF consists of inorg. salts and minerals such as calcium chloride, copper sulfate, sodium hydrogen phosphate, sodium sulfate, magnesium sulfate, potassium chloride, and zinc sulfate, amino acids, vitamins and other miscellaneous components. The addnl. components are **insulin**, fetuin, peptone, ferric citrate, and surfactant. **Insulin** and fetuin originated from cow is used and Pluronic F-68 is used as surfactant. LSF medium is used for expression of **erythropoietin** from transfected **CHO** cells and for the culture of **CHO** DUKX B1 and **CHO** DG44 cells. The cost of LSF medium is one half of conventional medium containing serum.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	KR 220090	B1	19991001	KR 1997-7188	19970305

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:164674 CAPLUS
DN 132:171061
TI Recombinant human erythropoietin with superior in vivo activity production in CHO cells
SO Braz. Pedido PI, 18 pp.

CODEN: BPXXDX

IN Paez Meireles, Rolando; Rodriguez Molto, Maria Pilar; Garcia del Barco Herrera, Diana; De la Fuente Garcia, Jose de Jesus; Tamayo, Caridad; Rodriguez Rodriguez, Elsa Maria; Rodrigues Mayon, Alina; Limonta Velazquez, Jose Manuel; Ruiz Hernandez, Odalys; Lopez Perea, Patricia

AB A process for production of human recombinant erythropoietin is disclosed which involves a cell-culture system which allows for production of 3 different batches of product free of serum, merely supplemented with insulin, followed by a simple process of purification, which includes a G-25 chromatog. step, an ion exchange (Q-Sepharose FF), hydrophobic interaction chromatog. (Bu TSK) and gel filtration. The recovery of erythropoietin is a process taking 15 days.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BR 9704975	A	19990525	BR 1997-4975	19971003

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S65	51	(US-6586398-$ or US-6548653-$ or US-6471500-$ or US-6399333-$ or US-6355241-$ or US-6048724-$ or US-5994127-$ or US-5955422-$ or US-5888772-$ or US-5756349-$ or US-5621080-$ or US-5618698-$ or US-5547933-$ or US-5441868-$ or US-4806524-$ or US-6376218-$ or US-5256294-$ or US-5789247-$ or US-6646120-$ or US-6555006-$ or US-6406623-$ or US-6387270-$ or US-6221249-$ or US-5490937-$ or US-4667016-$ or US-4703008-$). did. or (US-6696056-$ or US-4677195-$).did. or (US-20020012991-$ or US-20020146771-$ or US-20030175951-$ or US-20030178367-$ or US-20020108907-$).did. or (EP-513738-$ or WO-9214539-$ or WO-9742835-$ or EP-148605-$ or WO-9635718-$).did. or (JP-2003250533-$ or JP-05252942-$).did. or (BR-200107531-$ or WO-200028066-$ or WO-200027997-$ or WO-200027869-$ or WO-200027419-$ or US-20020086816-$ or CN-1190130-$ or BR-9704975-$ or US-6399333-$ or EP-513738-$ or EP-923308-$).did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/01/11 10:47
S77	3	Carcagno SAME miguel	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:03
S78	31	Carcagno	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:04
S79	314	recombinant NEAR erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:30
S80	247	S79 and (CHO COS BHK Namalwa HeLa)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:10
S81	117	S80 and glucose	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:10

S82	129	Koch stefan	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/01/10 11:30
S83	0	S82 and erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:32
S84	11	BEHRENDT WITH ulrich	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:32
S85	207	DMEM:F12	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:33
S86	45	S85 and erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:32
S87	32	S86 and glucose	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:32
S88	27041	DMEM	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:33
S89	58	S88 and S79	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:33
S90	42	S89 and glucose	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/10 11:33
S94	43631	ethanolamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/11 10:48
S95	1859	S94 and cho ADJ cells	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/11 10:48